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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/721,022	11/25/2003	Mary Ann Lukas-Laskey	04012.0384	3995

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/721,022	LUKAS-LASKEY ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 11, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-11-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Request for Continued Examination (RCE) filed October 11, 2006 is acknowledged and accepted. Claims 1-30 remain under consideration.

An Information Disclosure Statement filed October 11, 2006 is further acknowledged and has been reviewed.

The indicated allowability of claims 1-30 is withdrawn in view of reconsideration of references to Olsen et al., Journal of the American College of Cardiology, and Metra et al., Journal of the American College of Cardiology. Rejections based on these references follow.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 9 is rejected under 35 U.S.C. 102(a) as being anticipated by Metra et al. Journal of the American College of Cardiology. Metra teaches the oral administration of 6.25 mg of carvedilol twice a day for 7 days. See the Abstract under *Methods*. Metra teaches the addition of carvedilol to "standard therapy", which meets the limitation of claim 9 drawn to "in combination with at least one other therapeutic agent". The open language of claim 9, i.e., the recitation of "comprising," allows for the inclusion of additional therapeutic options.

Claim 9 is drawn to a method of treating to decrease a risk of mortality, comprising administering carvedilol once or twice daily, alone or in combination with at

least one other therapeutic agent for a period of 7 to 28 days. See the Abstract under *Conclusions* where Metra teaches the administration of carvedilol to both reduce heart rate and also mean pulmonary artery and pulmonary wedge pressures in the short-term, and, improve exercise left ventricular systolic function and reduce heart failure symptoms in the long-term. In patients with idiopathic cardiomyopathy, administration of carvedilol improves submaximal exercise tolerance. Accordingly, carvedilol clearly decreases a risk of mortality in patients who suffer from the inability of the heart to maintain adequate blood circulation in the peripheral tissues and the lungs, and in patients having the clinical syndrome that defines congestive heart failure, i.e., shortness of breath, pitting edema, enlarged tender liver, engorged neck veins and pulmonary rales.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 10-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olsen et al., Journal of the American College of Cardiology, and Metra et al., in view of Journal of the American College of Cardiology.

Olsen teaches the oral administration of an initial dose of 3.125 mg of carvedilol twice daily for one week to improve both symptoms of congestive heart failure and left ventricular function in patients with congestive heart failure. In a second phase of administration, 6.25 mg of carvedilol is given twice daily and titrated over one month to

a maximum dose of 25 mg twice daily for those patients weighing less than 75 kg and 50 mg twice daily for those patients weighing over 75 kg. In a third phase of administration, the dosing continued for three additional months. Accordingly, Olsen's teaching meets or suggests the dosing regimen requirements of claims 1, 7, 10, 20 and 26 with respect to the length of time of administration, the amount of drug given to patients and the daily administration requirements in each part of the triphasic claimed protocols. Metra provides a clear teaching drawn to a reduction in a risk of mortality in patients suffering from congestive heart failure. See the Abstract under *Conclusions* where Metra teaches the administration of carvedilol to both reduce heart rate and mean pulmonary artery and pulmonary wedge pressures in the short-term, and, improve exercise left ventricular systolic function and reduce heart failure symptoms in the long-term. In patients with idiopathic cardiomyopathy, administration of carvedilol improves submaximal exercise tolerance.

Therefore, in view of the combined teachings of Olsen and Metra, one skilled in the cardiology art would have been motivated to administer carvedilol in a treatment regimen that comprises a first dosage (3.125 mg or 6.25 mg or 10-30% of the daily maintenance dosage) at least daily for a period of 7 days, followed by a second dosage (12.5 mg or 20-70% of the daily maintenance dosage) for a period of 7 days to a month and finally a third dosage (10-100mg carvedilol) for a maintenance period. The actual determination of an optimal duration and dosage of each phase of therapy and, in particular, the maintenance phase, would reasonably be determined by the skilled practitioner in cardiology, in view of each individual patient's medical profile, through no

more than routine experimentation, and, in particular, in view of the guidelines provided by the prior art. The conclusions drawn by Metra's teaching provide a reasonable expectation of success in decreasing a risk of mortality caused by congestive heart failure.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel can be reached on 591-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

January 18, 2007

Phyllis G. Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER